UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,359	06/06/2006	Shirou Sawa	2006_0587A	6815

513 7590 06/02/2009

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
06/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,359	SAWA, SHIROU	
	Examiner	Art Unit	
	LAYLA BLAND	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 9, 2009 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed March 9, 2009, and amendment and response to the Final Office Action (mailed October 9, 2008), filed March 9, 2009 wherein claim 1 is amended.

Claims 1, 3, 4, and 6-9 are pending and are examined on the merits herein.

The following rejection is maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu (US 5,414,011, May 9, 1995, PTO-1449 submitted May 5, 2006) in view of Ogawa (US 4,910,225, March 20, 2990, PTO-1449 submitted May 5, 2006,

Cagle (US 6,440,964, August 27, 2002, of record) and Miyagi (US 6,281,224, August 28, 2001, PTO-1449 submitted May 5, 2008).

Fu teaches stable, clear ophthalmic formulations comprising a –COOH group-containing NSAID in combination with an antibiotic, a preservative, and a nonionic surfactant, all in an aqueous vehicle [see abstract]. Preferred embodiments comprise ketorolac (0.25-0.5% wt/vol.) and tobramycin (0.15-0.3% wt/vol.), as well as buffers and nonionic surfactants [columns 9 and 10, Examples 3-6]. Other suitable NSAIDs include indomethacin, flurbiprofen sodium, and suprofen [column 6, lines 9-16]. The formulations are prepared by dissolving the solutes in water and adjusting the pH to about 6-8 [column 6, lines 63-67]. Suitable buffers include citrate [column 6, lines 48-50]. The ophthalmic formulations can be administered in the form of an eye drop [column 8, lines 24-35].

Fu does not teach bromfenac as the NSAID and does not teach inclusion of monoethanolamine or nicotinamide in the formulation.

Ogawa teaches ophthalmic compositions comprising bromfenac (a –COOH group-containing NSAID) [see abstract and column 5, Test drug]. The concentration of the active ingredient in a liquid preparation is preferably 0.01-5% [column 4, lines 40-46]. Bromfenac has a strong anti-inflammatory effect than indomethacin [column 8, lines 1-2]. The solution is stabilized by the addition of a water-soluble polymer and by adjusting the pH [column 3, lines 12-15]. Buffer should be added to adjust the pH to about 6.0-9.0, preferably about 7.5-8.5 [column 3, lines 48-55]. A preferred water-soluble polymer is polyvinylpyrrolidone [column 3, lines 54-56]. The ophthalmic

composition may also include other anti-inflammatory agents and an antimicrobial [column 4, lines 1-5].

Cagle teaches that cyclooxygenase type I and type II inhibitors such as diclofenac, flurbiprofen, ketorolac, supfrofen, bromfenac, and indomethacin are preferred NSAIDs for use in ophthalmic formulations comprising an antibiotic and a non-steroidal anti-inflammatory agent [column 7, lines 49-58].

Miyagi teaches opthalmic solutions containing the NSAID pranoprofen (which is also a cyclooxygenase inhibitor) and an organic amine [see abstract]. Excellent stability and little irritation to the eyes can be prepared by the addition of organic amine [column 1, lines 59-63], preferably alkanolamines such as monoethanolamine [column 2, lines 3-5]. Surfactants such as polysorbate 80 can also be added [column 3, lines 11-40].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare an aqueous composition comprising tobramycin, bromfenac, and an alkanolamine. Bromfenac and other cyclooxygenase inhibitor NSAIDs are well known in the art for ophthalmic formulations. Aminoglycoside antibiotics such as tobramycin are also known for ophthalmic formulations. The use of aminoglycoside antibiotics along with NSAIDs is also known in the art. Ogawa teaches that polyvinylpyrrolidine can be used to help stabilize an ophthalmic solution, and Miyagi teaches that monoethanolamine can also be used to stabilize an ophthalmic solution and to reduce eye irritation. Thus, the prior art includes each element currently claimed, and each element in the combination would be expected to perform the same function

as each did separately. Thus, the skilled artisan could have recognized that these elements could be combined and that the results would be predictable.

Response to Arguments

Applicant argues that the cited references do not disclose or suggest that turbidity and suspension formation occurs in aqueous solutions comprising bromfenac and an aminoglycoside antibiotic, or that a clear solution can be obtained by adding monoethanolamine or nicotinamide. This argument has been fully considered but is not persuasive. Monoethanolamine is disclosed as a stabilizer and as a means to make an ophthalmic composition less irritable to the eye, which are two reasons for the skilled artisan to incorporate it in an ophthalmic composition. Miyagi's teaching of stability could be interpreted as physical stability and thus Miyagi does suggest that precipitation or other undesirable physical transformations are inhibited by monoethanolamine. Furthermore, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant argues Cagle recites a large number of NSAIDs and it would have been inconceivable to select bromfenac from among them. Cagle was cited simply to show that the prior art recognizes that cyclooxygenase type I and type II inhibitors such as diclofenac, flurbiprofen, ketorolac, supfrofen, bromfenac, and indomethacin can be used interchangeably in an ophthalmic composition. Fu teaches a composition

comprising the above NSAIDs and an aminoglycoside antibiotic; thus the skilled artisan would expect bromfenac and an aminoglycoside antibiotic to be a successful combination because bromfenac is of the same class as the compounds used by Fu and can be used interchangeably with those NSAIDs in an ophthalmic composition, as taught by Cagle.

Applicant argues that Miyagi uses tromethamine to obtain a clear solution, not monoethanolamine. However, Miyagi also teaches monoethanolamine as a preferred alkanolamine, so the skilled artisan would have a reasonable expectation that monoethanolamine would be effective.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, the above rejection is based only upon knowledge which was contained within the cited references. Thus, Applicant's argument is not persuasive.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623